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EXAMINER	
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ART UNIT	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/589,469	MERIZZI, GIANFRANCO	
	Examiner	Art Unit	
	Paul Zarek	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 June 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-8,11 and 12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-8, 11, 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claims 1 and 3-8 have been amended, Claims 11 and 12 have been added, and Claims 2, 9, and 10 have been cancelled by the Applicant in correspondence filed on 06/24/2009. Claims 1, 3-8, 11, and 12 are currently pending. This is the second Office Action on the merits of the claim(s).

RESPONSE TO ARGUMENTS

2. Claims 1-8 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite because the rejected claims provide for the use of a compound of formula (I), (II), or (III), but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. This rejection is moot in light of Applicant's amendment to the claims.

3. Claim 6 was rejected under 35 U.S.C. 112, second paragraph, as being indefinite because it lacked antecedent basis. This rejection is moot in light of Applicant's amendment to Claim 6.

4. Claim 8 was rejected under 35 U.S.C. 112, second paragraph, as being indefinite for containing both a broad and narrow limitation. This rejection is moot in light of Applicant's amendment to Claim 8.

5. Claims 1-8 were rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for Parkinson's disease and ischemia/reperfusion injury, does not reasonably provide enablement for treating a disease or pathology not associated with

Parkinson's disease or ischemia/reperfusion, or prevention of any disease or pathology. Claims 1 and 3-8 are considered enabled only for the treatment of Parkinson's disease and ischemia/reperfusion injury. Examiner notes that "treating" also encompasses "preventing" (pg 10, lines 4-5). Amended Claims 1 and 3-8 encompass treating and preventing all neurodegenerative diseases. Applicant has not disagreed with the content of this rejection. Applicant's amendment to Claims 1 and 3-8 do not overcome this rejection. Therefore, the rejection of Claims 1 and 3-8 35 U.S.C. 112, first paragraph, is maintained.

6. Claims 1 and 5-10 were rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the composition of formula (I) and use thereof wherein R_1 and R_2 are hydrogen, C_1-C_{12} alkyl, C_2-C_{12} alkenyl, and C_2-C_{12} alkynyl, does not reasonably provide enablement for a composition of formula (I) or use thereof wherein R_1 and R_2 together form a tetramethylene or pentamethylene group. This rejection is moot in light of Applicant's amendment to Claims 1 and 5-8 and cancellation of Claims 9 and 10.

7. Claims 1-8 were rejected under 35 U.S.C. § 101 because the claims were drawn to a nonstatutory category. This rejection is moot in light of Applicant's amendment to Claims 1 and 3-8 and cancellation of Claim 2.

8. Claims 1-4 and 7-9 were rejected under 35 U.S.C. 102(b) as being anticipated by Paolini and Pedulli (US Patent no. 5,981,548, issued 1999). This rejection is moot in light of Applicant's amendment to Claims 1, 3, 4, 7, and 8, and cancellation of Claims 2 and 9.

9. Claim 10 was rejected under 35 U.S.C. 103(a) as being unpatentable over Paolini and Pedulli (above). This rejection is moot in light of cancellation of Claim 10.

10. Claims 5 and 6 were rejected under 35 U.S.C. 103(a) as being unpatentable over Paolini and Pedulli, and further in view of Ito, et al. (European Application EP 1 132 085, published 2001), Floyd, et al., (US Patent no. 5,036,097, issued 1991), and Atlas, et al. (US Patent no. 6,420,429, issued 2002). Applicant traversed this rejection on the grounds that these prior art do not teach or fairly suggest the claimed method of treating a neurodegenerative disease comprising a compound of formula (I), (II), or (III). Specifically, Applicant states that nothing in the prior art disclose that the claimed compound is able to cross the blood-brain barrier (BBB). Applicant then asserts that nothing in Ito, et al., Floyd, et al., or Atlas, et al., indicate that the compounds of Paolini and Pedulli would be capable of crossing the BBB, and that even if a compound could cross the BBB, it would not necessarily be sufficient to treat Parkinson's disease. For these reasons, Applicant contends that the claimed method of treating a neurodegenerative disease is not *prima facie* obvious over the prior art. Examiner respectfully disagrees.

11. There is no limitation within Claims 5 and 6 that the any of the claimed compounds must cross the BBB. All that is required is that the claimed compounds are administered in an effective amount. "Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993)" (MPEP 2145(VI)). The claimed compounds could be administered intrathecally or intracranially, thereby by-passing the BBB altogether. Applicant's contention that none of the prior art teach that all oxygen scavengers would necessarily be therapeutic for Parkinson's disease is not persuasive. The test is whether one of ordinary skill in the art would reasonably expect the claimed method would be therapeutically efficacious. Atlas, et al., discuss

that vitamin E is not effective for treating Parkinson's disease because it gets trapped in the cell membranes. Vitamin C is not effective because it is unable to cross the BBB (col 4, lines 6-17). Paolini and Pedulli teach that the compounds disclosed therein, which encompass instantly claimed formula (I), "hav[e] high lipophily allowing said compound to easily pass through the double lipoproteinic layer of the biological membranes, obtaining thereby a high concentration of active substance in the body area where anti-radical protection is required." (col 2, lines 44-48). Thus, Paolini and Pedulli, teach that the compounds of formula (I) are both oxygen scavengers and are capable of entering into cells. The combination of Ito, et al., Floyd, et al., and Atlas, et al., provide a motivation to use the compounds of Paolini and Pedulli, for treating ischemia/reperfusion injury and Parkinson's disease (see previous Office Action, pg 11 para 15). Therefore, the rejection of Claims 5 and 6 under 35 U.S.C. 103(a) as being unpatentable over Paolini and Pedulli, and further in view of Ito, et al., Floyd, et al., and Atlas, et al., is maintained. Applicant's amendment to Claims 5 and 6 do not overcome this rejection.

12. Amended Claims 1, 3, 4, 7, and 8 and newly added Claims 11 and 12 are examined on their merits and the following **FINAL** rejection is made.

Claim Rejections - 35 USC § 112 (2nd paragraph)

13. The text of Title 35, U.S.C. § 112, second paragraph, can be found in a prior Office action.

14. Claim 6 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the

invention. Claim 6 recites the limitation, "The method of a compound". It is unclear what this mean. Therefore, Claim 6 is considered indefinite. Applicant may overcome this rejection by amending Claim 6 to read, "The method according to Claim 1."

Claim Rejections - 35 USC § 112 (1st paragraph)

15. The text of Title 35, U.S.C. § 112, first paragraph, can be found in a prior Office action.

16. Claims 11 and 12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating Parkinson's disease or ischemia/reperfusion injury, does not reasonably provide enablement for preventing Parkinson's disease or ischemia/reperfusion injury. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The reasons for lack of enablement were described in previous Office Action and are applied in the same capacity here.

Claim Rejections - 35 USC § 103

17. The text of Title 35, U.S.C. § 103(a) can be found in a prior Office action.

18. Claims 1, 3, 4, 7, 8, 11, and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Paolini and Pedulli (above), in view of Ito, et al. (above), Floyd, et al. (above), and Atlas, et al. (above).

19. Amended Claim 1 is drawn to a method of treating a neurodegenerative disease comprising administration of an effective amount of formula (I). Claims 3 and 4 limit the substituents R_1, R_2, R_3, R_4, R_5, R_6, and R_7 of formula (I). Claim 7 further limits the claimed

formulae to be in a pharmaceutical or veterinary composition suitable for oral, parenteral, inhalatory or topical administration. Claim 8 further limits the claimed formulae to be in a dosage form suitable for administration in quantities of between 0.01-200 mg/kg body weight. Claim 11 limits the neurodegenerative disease and compound of Claim 1 to Parkinson's disease or ischemia/reperfusion injury and bis(1-oxyl-2,2,6,6-tetramethyl-4-piperidinyl)decandioate or bis(1-hydroxy-2,2,6,6-tetramethyl-4-piperidinyl)decandioate, respectively. Claim 12 limits the dose of Claim 8 to range between 0.5 and 20 mg/kg body weight.

20. Paolini and Pedulli teach a composition identical to formula (I) that contains identical substituents of the instant application. Paolini and Pedulli also teach compositions suitable for oral and parenteral administration (col 7, lines 20-30), and a single dose of 1-100 mg (col 7, lines 46-47). Although Paolini and Pedulli do not teach the dose normalized to body weight, the range taught in this prior art falls within the range of Claim 8. Paolini and Pedulli teach composition of formula (I) wherein both R_6 and R_7 are hydroxyl. However, it is known that the oxygen of a hydroxyl group, when in solution, can lose the hydrogen to become an oxyl group. Therefore, the compound of Claim 11 is a *prima facie* obvious variant of the composition taught by Paolini and Pedulli. Paolini and Pedulli do not teach a method of treating a disease with formula (I).

21. Ito, et al. teach that oxygen free radicals cause various *in vivo* reactions including ischemic disease and nervous disease accompanied by nerve degeneration (paragraph 0004). Floyd, et al., teach that oxygen scavengers are therapeutically effective for the treatment of ischemia/reperfusion (col 2, lines 11-15). Atlas, et al., teach that oxygen scavengers are therapeutically effective for the treatment of Parkinson's disease (col 4, lines 40-44).

22. As discussed above, Applicant's arguments with respect to the ability of the compounds of Paolini and Pedulli not being disclosed to cross the BBB is not found persuasive as there is no limitation in any of Claims 1, 3, 4, 8, 11, or 12 that the compounds must cross the BBB. Applicant's arguments that these prior art do not definitively state that all oxygen scavengers would be therapeutically efficacious for the treatment of Parkinson's disease or ischemia/reperfusion injury is not considered persuasive. As discussed above, Paolini and Pedulli disclose that the compounds disclosed therein, which overlap with the claimed compounds of formula (I), are effective in getting into a cell to exert their anti-oxidant effects. Given that Paolini and Pedulli teach that the compounds of formula (I) can cross the cell membrane and that Ito, et al., Floyd, et al., and Atlas, et al., teach that oxygen scavengers are therapeutically effective for the treatment of ischemia/reperfusion injury (Floyd, et al.) and Parkinson's disease (Atlas, et al.), it would have been *prima facie* obvious to treat Parkinson's disease and/or ischemia/reperfusion injury with the compounds of formula (I).

23. Instant Claim 7 limits the dosage form of formula (I) to be suitable for oral, parenteral, inhalatory or topical administration. For this claim, the ability of formula (I) to cross the BBB is germane. Applicant asserts in reply filed on 06//24/2009 that he has unexpectedly found that the compounds of formula (I) cross the BBB. Applicant has provided no data or reference indicating that the ability of the compounds of formula (I) to cross the BBB is unexpected.

24. Paolini and Pedulli teach that the compounds disclosed therein, which encompass instantly claimed formula (I), would be useful for the treatment of various diseases, including hyperbaric damage affecting the central nervous system (col 6, lines 39-40). This suggests that the compounds disclosed by Paolini and Pedulli are capable of crossing the BBB to affect their

anti-oxidant effects on the CNS. Wilkinson (Goodman & Gilman's The Pharmacological Basis of Therapeutics, 10th ed., 2001) teaches that the more lipophilic a compound it the more likely it will be capable of crossing the BBB (pg 10, col 2, lines 11 and 12). Paolini and Pedulli teach that the compounds disclosed therein are lipophilic (col 10, lines 7-9; Figure 5). Given the known lipophilicity of the formula (I), one of ordinary skill the art would reasonably expect these compounds to cross the BBB. Moreover, crossing the BBB may not even be necessary. Bloom (Goodman & Gilman's The Pharmacological Basis of Therapeutics, 10th ed., 2001) teaches that cerebral ischemia modifies the BBB to increase access of substances (i.e. compounds of formula (I)) to the CNS (pg 297, col 2, lines 17-20).

25. For these reasons, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to treat Parkinson's disease and/or ischemia/reperfusion injury with compounds of formula (I).

Conclusion

26. Claims 1 and 3-8 remain rejected. Newly added Claims 11 and 12 are rejected.

27. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

28. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Paul Zarek whose telephone number is (571) 270-5754. The examiner can normally be reached on Monday-Thursday, 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

PEZ

/San-ming Hui/
Primary Examiner, Art Unit 1617